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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/609,721	06/30/2000	Mark S. Dennis	PI713R1	2692

7590                    01/15/2002  
Jeffrey S kubinec  
1 DNA Way  
South San Francisco, CA 94080

EXAMINER /

JIANG, DONG

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 01/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/609,721	DENNIS, MARK S.	
	<b>Examiner</b> Dong Jiang	<b>Art Unit</b> 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 15 November 2001.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-10 and 21-40 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-10 and 21-40 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
 If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
  - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                               | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>2 and 4</u> . | 6) <input type="checkbox"/> Other: _____                                    |

**DETAILED OFFICE ACTION**

Applicant's amendment and election with traverse of SEQ ID NO:14 in Paper No. 7, filed on 15 November 2001 is acknowledged. The traversal is on the ground(s) that the pending claims related to a peptide containing a common sequence motif, and that claims encompassing the motif can be examined in a single application without an undue burden on the Office. This argument is persuasive, and requirement for the species restriction is withdrawn. Following the amendment, claim 11-20 are canceled, claims 1-10, 21, and 30 are amended, and the new claims 39 and 40 are added.

Currently claims 1-10, and 21-40 are pending and under consideration.

**Formal Matters:**

Claim 23 is objected to for depending on a canceled claim, claim 20. The applicant is required to amend the claims to read only upon the pending claims.

**Objections and Rejections under 35 U.S.C. 112:**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 22-26, and 33-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it is unclear what is intended by "a non-naturally occurring" peptide ligand. "Isolated" or "purified" is suggested.

Claims 2 and 33 are indefinite because it is unclear which peptide ligand is intended as the claims are dependent from claim 1, which recites two "peptide ligand".

Claims 5, 6, 7 are indefinite because the definition of Xaa<sub>1</sub> is not consistent with that in claim 1 from which claims 5, 6, 7 are dependent.

Claims 6-10 are similarly indefinite, wherein the definition of Xaa<sub>3</sub> is not consistent with that in claim 1.

Claim 22 is indefinite because it is unclear where “a linker sequence” is located, could it be inserted *in* the sequence of claim 21?

Claim 35 recites the limitation “the control sequence” in line 2. As the claim depends from claim 33, and there is no such term in claim 33, therefore, there is insufficient antecedent basis for this limitation in the claim.

Claim 37 is indefinite for the recitation of “expressing *a DNA* molecule encoding *a peptide ligand*”. It is unclear what it is meant by the term, as the cells may express peptide ligands other than said specific peptide ligand.

Claim 39 is indefinite because it is unclear whether “a functional moiety” is “linked to” the peptide ligand or to the 1-7 amino acids of Xaa<sub>3</sub>.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 33-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-10 and 33-38 are directed to a non-naturally occurring peptide ligand which competes for binding HER2 in an in vitro assay with a peptide ligand having SEQ ID NO:90.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed.*” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NO:90, which would compete with itself in an in vitro assay, the skilled artisan cannot envision the detailed chemical structure of the encompassed

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peptide ligands, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, no non-naturally occurring peptide ligand except that having the amino acid sequence set forth in SEQ ID NO:90 meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The broad genus claim is represented by *one* molecular species described with particularity in the disclosure, the peptide ligand having SEQ ID NO:90. No other peptide ligand, or species meeting the limitations of the claims is identified or particularly described. The Examiner, therefore, concludes that the one species of the HER2 peptide ligand, which would compete with itself in an in vitro assay is not likely to be representative of all species recited in claim 1, and thus that the disclosure does not convey to those skilled in the art that the inventors were in possession of the genus of all HER2 peptide ligands at the time the application was filed.

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 30 is directed to a pharmaceutical composition comprising the formulated peptide ligand, which indicates a therapeutic application of the composition. Although the prior art indicates a direct role for HER2 in the pathogenesis and clinical aggressiveness of HER2-

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overexpressing tumors, and HER2 as a predictor of a poor prognosis in certain malignancies, the specification provides no actual experiment result of any kind to indicate the in vivo application of the claimed peptide ligand. Further, the specification provides no guidance, nor working example as to how to use the claimed invention. The evidence of in vitro binding of the peptide ligand to HER2 is, by itself, insufficient because a binding ligand can be an agonist or antagonist of a given receptor, it is unpredictable that the present peptide ligand is an antagonist of HER2 without experimental evidence to confirm such. And therefore, the skilled artisan would not accept that the said peptide ligand would be beneficial to those individuals indicated in the prior art. Undue experimentation is required to determine such.

**Rejections Over Prior Art:**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 1 and 30 are rejected under 35 U.S.C. 102(b) as anticipated by, or, in the alternative, under 35 U.S.C. 103(a) as obvious over Jessell et al., US 5,279,966.

Claim 1 requires the functional limitation that a non-naturally occurring peptide ligand competes for binding HER2 with a peptide ligand having the stated formula, which apparently has a property of binding to HER2. Such a peptide would be expected to be able to compete with itself in an in vitro assay. The reference teaches an amino acid sequence (SEQ ID NO:15), which comprises the amino acid sequence identical to that in the formula of claims 1 and 30 of the instant application (see appended computer printout of sequence search results), and a pharmaceutical composition thereof (the abstract, the last 5 lines), but does not mention the HER2 binding property as claimed. The examiner is unable to determine whether the prior art disclosure possesses the non-recited property. With these conditions, where the prior art peptide comprises the amino acid sequence that seems to meet the sequence limitation of the formulated peptide of claim 1 (and 30), and could be able to compete with the formulated peptide in an in vitro assay except that the prior art is silent to the HER2 binding property claimed, then the burden shifts to the applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Claims 21-29, 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jessel et al., US5,279,966, in view of Capon et al., US5,116,964.

Jessel discloses an amino acid sequence (SEQ ID NO:15), which comprises the amino acid sequence in part (a) of claim 21 in the instant application (see appended computer printout of sequence search results).

The primary reference does not teach a recombinant fusion polypeptide comprising a linker sequence, an immunoglobulin constant region sequence.

Capon discloses a novel polypeptide comprising an immunoglobulin Fc region, and a target protein sequence (column 5, lines 13-20). The cited reference indicates that fusion of a target protein to a stable plasma protein such as an immunoglobulin constant domain extends the in vivo plasma half-life, and facilitate purification of the protein (column 4, lines 38-43, and column 5, lines 13-20). Additionally, Capon suggests that the fusions may be modified by

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linking them through peptidyl or in vitro generated bonds to an additional therapeutic moiety such as a polypeptide toxin, or other functionality (column 5, lines 56-60), and that they may be purified and formulated in pharmacologically acceptable vehicles for therapeutic applications (column 6, lines 6-8). Furthermore, the reference teaches that the fusions retain at least functionally active hinge, CH<sub>2</sub> and CH<sub>3</sub> domains of the constant region of an immunoglobulin heavy chain (column 10, lines 10-12).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the amino acid sequence of Jessel et al., which meets the limitations of part (a) in claim 21, to make a fusion polypeptide comprising said peptide and an Ig constant region sequence as taught by Capon. One of ordinary skill in the art would have been motivated to make such a fusion polypeptide (as claims 21, 23-26), or a fusion polypeptide further comprising an additional functional moiety, such as a cytotoxic agent (as in claims 27-29, 31, and 32) for the treatment as Jessell suggested (the abstract, lines 12-15, and column 9, the first paragraph), because it would prolong in vivo plasma half-life, and confer or increase the therapeutic value to the peptide as suggested by Capon (column 5, lines 56-60), and reasonably would have expected success in view of Capon's disclosure, in which various genes had already been expressed successfully in their systems at the time the invention was made.

Capon does not specifically teach a linker (as claim 22). However, the reference suggests that the precise site at which the fusion is made is not critical, and may be determined by routine experimentation (column 10, lines 21-22). Additionally, it is well known in the art that an optional linker sequence may be used for making fusion proteins. Therefore, the claim merely recites the obvious employment of a well-known practice.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Hastings et al. (US 5,871,969) discloses a human neuronal attachment factor-1 with an amino acid sequence of 52 residues, which comprises a sequence of Cys-Xaa-Gly-Pro-Gly-Cys, wherein Xaa is Met. (see computer printout of the search results).

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Lippman et al. (US 5,869,618) discloses a 30 kDa TGFa-like glycoprotein which binds to the erbB2 oncogene product (HER2), and a method for stimulating and/or inhibiting the growth of cells which overexpress the human oncogene erbB-2.

**Conclusion:**

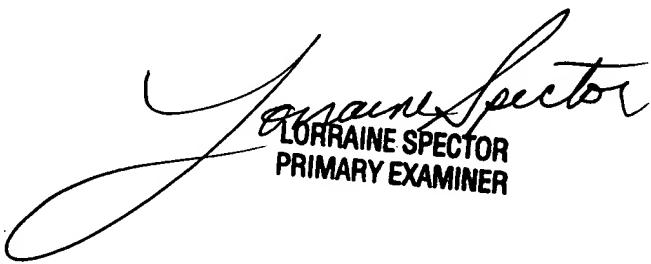
No claim is allowed.

**Advisory Information:**

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Lorraine Spector  
LORRAINE SPECTOR  
PRIMARY EXAMINER

DJ  
1/6/02